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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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[REDACTED] EXAMINER

CEPERLEY, MARY

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1641

DATE MAILED: 06/04/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/820,210	WAGNER ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Mary (Molly) E. Ceperley	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 14 March 2003.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-77 is/are pending in the application.
- 4a) Of the above claim(s) 3,6-8,11,13-23,25,28,30,32,33 and 35-77 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,2,4,5,9,10,12,24,26,27,29,31 and 34 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                    | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                           | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4,9</u> . | 6) <input type="checkbox"/> Other: _____ .                                   |

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**1)** Applicants' election without traverse of Group I, claims 1-13, 24, 26, 27, 29, 31, and 34, as further defined by the species IA in Paper Nos. 6 and 8 filed January 27, 2003 and March 12, 2003, respectively, is acknowledged.

Claims 14-23, 25, 28, 30, 32, 33, 35-77 are withdrawn from further consideration as being drawn to non-elected inventions.

Claims 3, 6-8, 11, and 13 are withdrawn from further consideration as not being readable on the elected invention, i.e. the elected species of formula IA.

Claims 1, 2, 4, 5, 9, 10, 12, 24, 26, 27, 29, 31, and 34 are treated on the merits in this Office action to the extent that they encompass the elected invention as defined by formula IA (March 12, 2003 response).

**2)** Claims 1, 2, 4, 5, 9, 10, 12, 13, 24, 26, 27, 29, 31, and 34 are rejected under judicially created doctrine as being drawn to an improper Markush group. To constitute a proper Markush group, the members of the group must (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility (MPEP 803.03). The compounds encompassed by formula (I) of claim 1 do not share any such substantial structural feature. The heterofunctional crosslinking reagent of claim 1, formula (I) is comprised of a "covalent core component" defined as "W" attached to three linking groups "L<sup>1</sup>", "L<sup>2</sup>", and "L<sup>3</sup>". The core component "W" includes essentially any and all trivalent moieties including, for example, the nitrogen atom *per se*, tridentate dendrimers, macrocyclic heterocycles, sugars, amino acids, phosphorus compounds, trivalent metals and hydrocarbons. These moieties contain no structural feature in common. A reference which would anticipate or render obvious a reagent containing one type of moiety (e.g. "W" defined as nitrogen) would not necessarily render obvious another reagent containing a different type of moiety (e.g. "W" defined as a sugar). Therefore, the Markush group defined by formula (I) is considered to be improper.

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The subgenus defined as W = amino acids (suggested by applicants in the March 12, 2003 response) does not define a group of compounds which share a substantial structural feature disclosed as being essential to the disclosed utility. The common core of the amino acid structure –CH(COOH)NH has not been disclosed as being essential to the disclosed utility. Further, for example, a reference which would anticipate or render obvious a reagent containing the simplest amino acid, glycine, as a core W, would not necessarily render obvious a reagent containing the heterocyclic ring-containing histidine or tryptophan as a core.

**3)** Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

**4)** The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**5)** The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**6)** Claims 1, 2, 4, 5, 9, 10, 12, 24, 26, 27, 29, 31, and 34 are rejected under 35 USC 112, second paragraph, as being indefinite for the following reasons.

**a)** In claim 1, in the absence of structural definitions, the terms "X", "Y", and "Z" render the claim indefinite since it is unclear what is meant to be encompassed by these terms. Further, in the absence of a description of what moieties are being "crosslinked", it is unclear what is meant by the terms "activatable covalent crosslinking group" and "protected or unprotected chemical crosslinking

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group". It is also unclear under what conditions the crosslinking group "Y" is "activatable" and what "Z" is being "protected" against.

**b)** The term "W" is a covalent core component" renders claim 1 indefinite for the reason that the required structural and functional features of this moiety are undefined.

**7)** Claims 1, 2, 4, 5, 9, 10, 12, 24, 26, 27, 29, 31, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation and use of certain "heterofunctional crosslinking reagents" *in the context of a specific method of use*, does not reasonably provide enablement for the entire scope of reagents of formula I as defined in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following limitations which are not present in claim 1, are requirements for the invention as it is described in the specification:

---"Y is an activatable...covalent crosslinking group adapted to link the heterofunctional crosslinker covalently at or adjacent the specific region or regions (?) of the protein" (page 2, lines 18-20). {It is unclear what the "specific region(s)" are and where they are located.}

---"Z" is the moiety of the "heterofunctional crosslinking reagent" which attaches to a label or solid support (Figure 1). "Z" does not serve the purpose of "crosslinking" (claim 1) as the term "crosslinking" is conventionally used in the art, i.e. multiple attachments between moieties.

**8)** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**9)** The rejections set forth below do not imply that a complete search has been made of the Markush group of formula (I) of claim 1.

**10)** Claims 1 and 2 are rejected under 35 USC 102(b) as being anticipated by Roberts et al (Basic Principles of Organic Chemistry, second edition, (1977)), 1208-1210).

The trifunctional amino acids (e.g. cysteine, threonine, serine, aspartic acid, etc.) anticipate the compounds of formula (I) of claim 1. For example, cysteine reads on the compound of formula (I) wherein W = -CH-, X = -CH<sub>2</sub>SH; Y, Z = -NH<sub>2</sub>, -COOH; L<sup>1</sup>-L<sup>3</sup> = a bond; serine reads on the compound of formula (I) wherein W = -CH-; X, Y, Z = -OH, -COOH, NH<sub>2</sub>; L<sup>1</sup>-L<sup>3</sup> = a bond.

**11)** Claims 1, 2, 4, 9, 12, 24, 26, 29, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Inman et al (U.S. 5,444,150).

The trifunctional compounds of Inman et al described at col. 6, lines 43-54 anticipate the compounds of instant claim 1 (see also, col. 7, lines 53-64). The Inman et al compounds correspond to the compounds of instant claim 1 wherein Br = X (a protein tag binder reactive with -SH); Y, Z = -COOH, CH<sub>3</sub>-C(CH<sub>3</sub>)<sub>2</sub>-O-C(O)-NH-; W = alanyllysine. For the limitation X = peptide of instant claim 9, see claim 3 of Inman et al. For the limitation Z = a reactive ester of claim 12, see the ester -O-C(O)-NH- of the formula of col. 6, lines 43-54 of Inman et al. For the reporter/label/support of claims 24, 26, 29, and 31 see Inman et al, claims 4 and 6-8 which contain an additional conjugated material such as a peptide, protein, ceramic, glass, or sugar.

**12)** Claims 1, 2, 4, 5, 9, 12, 24, 26, 29, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Oh et al (U.S. 5,851,778). The trifunctional (tridentate) compounds described in Figures 7 and 9 and at col. 13, line 59 through col. 14, line 13 and at col. 19, line 52 through col. 20, line 6 anticipate the trifunctional reagents of instant claim 1. For the attachment of reporters/labels/supports of instant claims 24, 26, 29, and 31, see Examples 7-9 of the reference.

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**13)** If the variables "Y" and "Z" were to be appropriately defined in the context of the method in which the "heterofunctional crosslinking reagent" of claim 1 is intended to be used (note paragraph **7**) above), a claim limited to the reagent of elected formula (IA) wherein W = glycinyl, L<sup>1</sup> is dicarbonylethyl, L<sup>2</sup> is 1,10-diaminodecanyl, and L<sup>3</sup> is methanethiolyl would be free of the prior art and would be allowable.

**14)** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. (Molly) Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached at (703) 305-3399. The fax phone number for responses to be filed BEFORE final rejection is (703) 872-9306. The fax phone number for responses to be filed AFTER final rejection is (703) 872-9307.

Questions which are NOT RELATED TO THE EXAMINATION ON THE MERITS, should be directed to **TC 1600 CUSTOMER SERVICE** at **(703) 308-0198**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

May 29, 2003

*Mary E. Ceperley*  
Mary E. (Molly) Ceperley  
Primary Examiner  
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